



Bilirubin metabolism and Jaundice-2

By

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INTENDED LEARNING OBJECTIVES (ILOs)



By the end of this lecture the student will be able to:

- 1. Distinguish different types of jaundice**
- 2. Interpret laboratory findings of different types of jaundice**



Outlines

What are different types of jaundice

Prehepatic jaundice

Hepatic jaundice

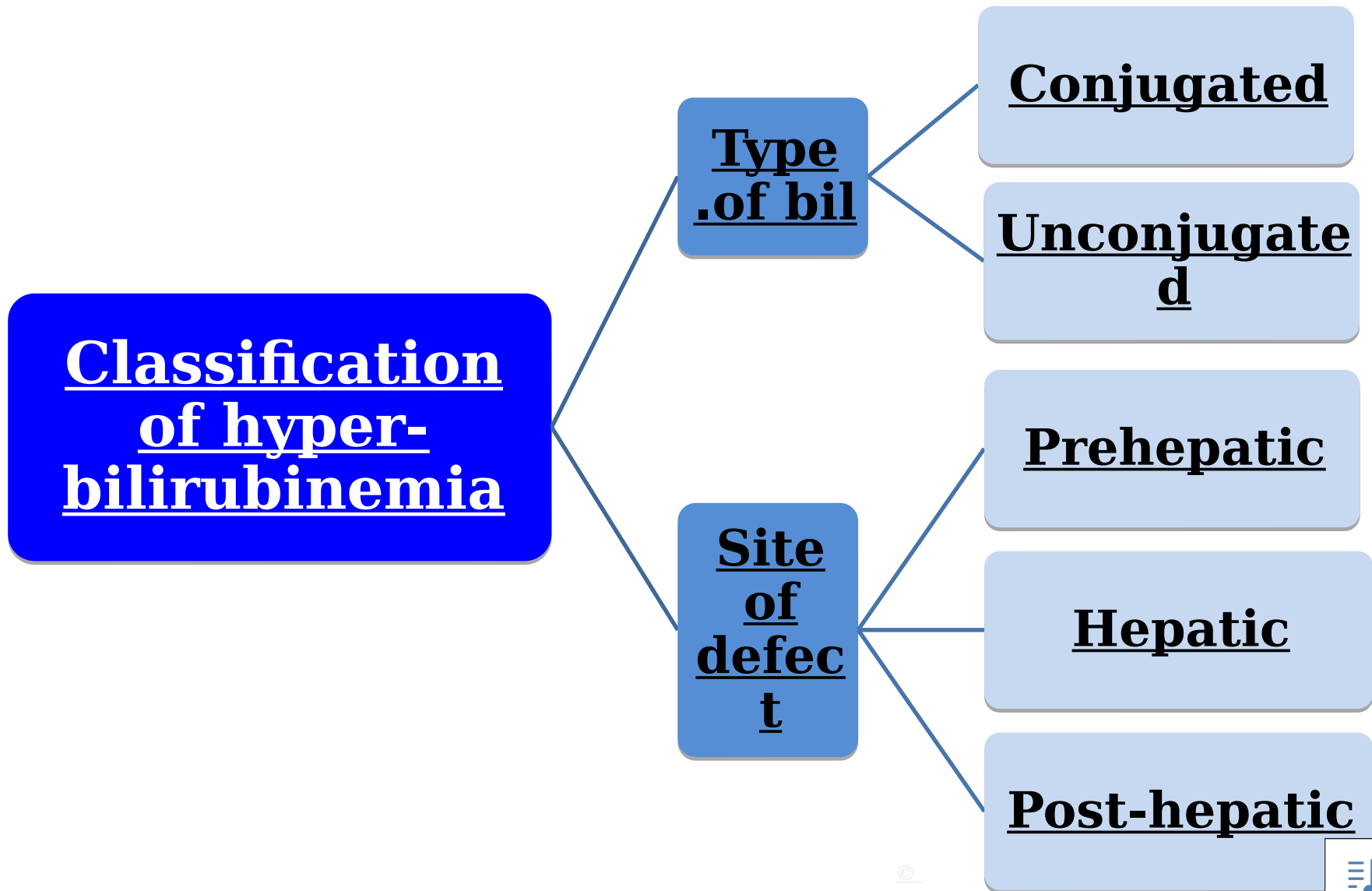
Post-hepatic jaundice



JAUNDICE



What are different types of jaundice



Classification of hyper-bilirubinemia according to site of defect

A- Prehepatic

Hemolytic

Neonatal jaundice

B- Hepatic

Hepatocellular damage

Crigler-Najjar syndromes I & II

Gilbert syndrome

Dubin-Johnson syndrome

Rotor syndrome

C- Post-hepatic

Obstruction of the biliary tree



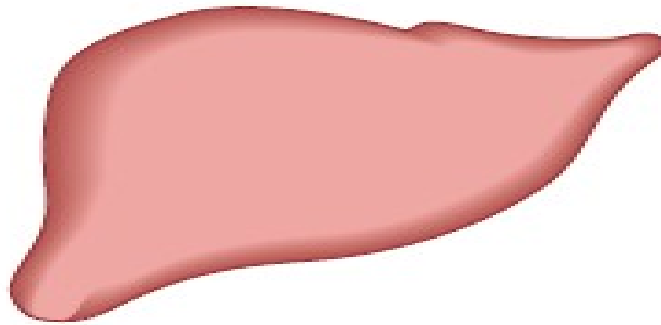
Classification of hyper-bilirubinemia according to site of defect

PRE-HEPATIC
(Vascular)



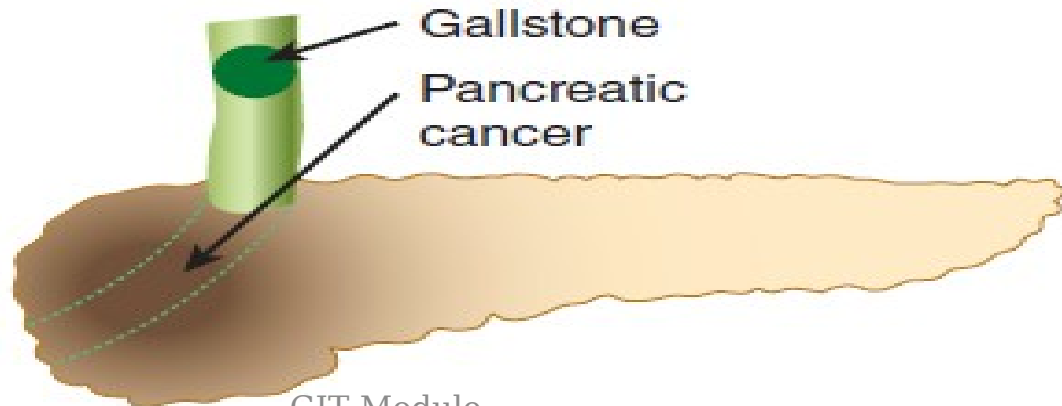
Hemolytic anemias

HEPATIC
(Liver)



Liver diseases
(eg, hepatitis, cancer)

POST-HEPATIC
(Biliary system &
pancreas)



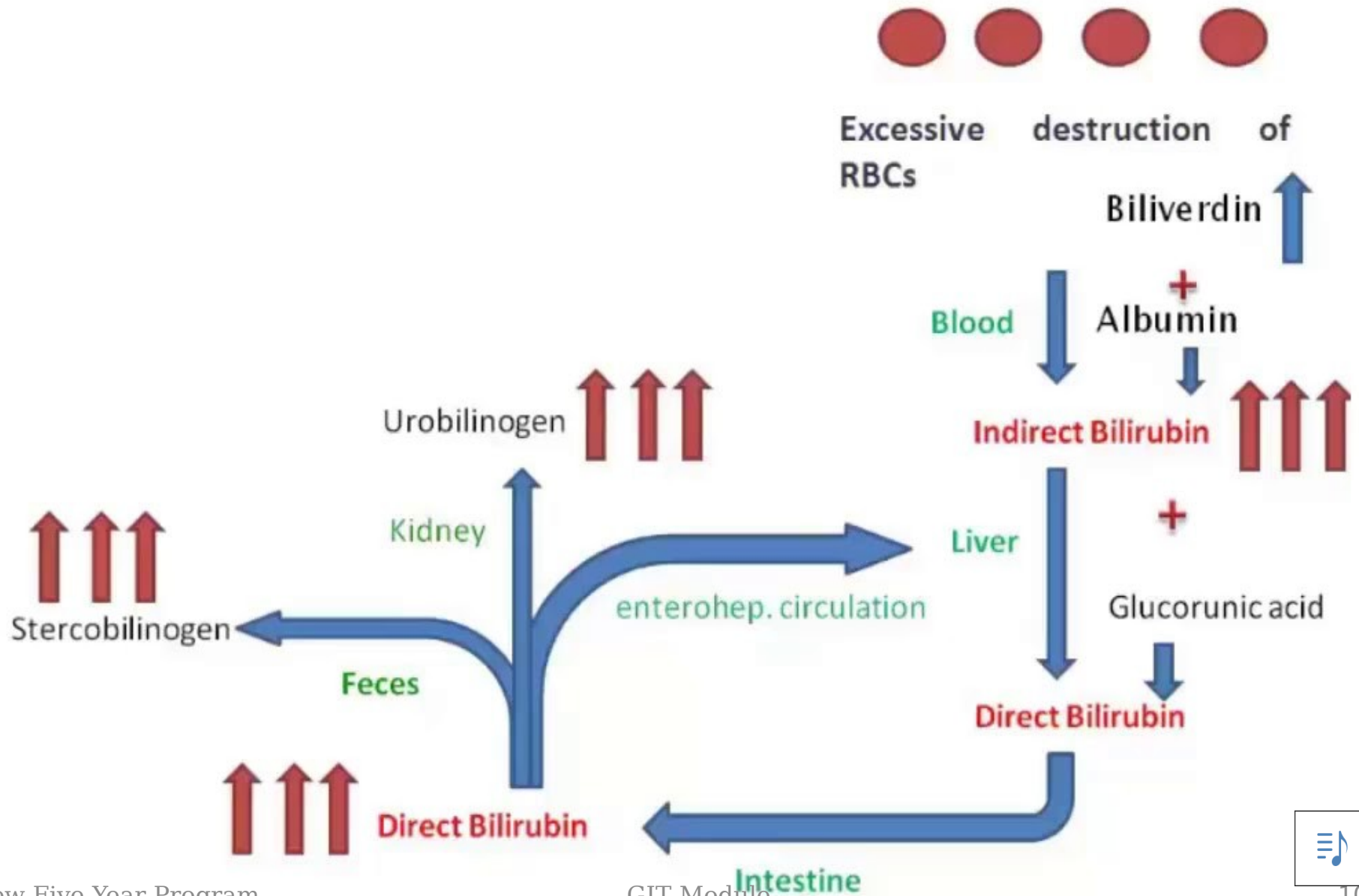
A- Prehepatic Jaundice

**Hemolytic -1
jaundice**

Neonatal jaundice -2



1) Hemolytic Jaundice

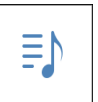


1- Hemolytic Jaundice (Retention hyperbilirubinemia)

Due to overproduction of bilirubin

Causes:

- **In neonates: Rh incompatibility between maternal and fetal blood.**
- **In children and adults: e.g G-6-PD deficiency, or pyruvate kinase deficiency or sickle cell anemia.**



1- Hemolytic Jaundice

Extensive hemolysis produce bilirubin **faster** than it can be conjugated:

- **UCB** in the blood **increases**,
- **More CB** is made and excreted into the bile,
- The amount of **urobilinogen** entering the enterohepatic circulation is **increases**
- Urinary **urobilin** and **stercobilin** **increases**



Jaundice, normal color of urine and stool



2- Neonatal “Physiological Jaundice”

**Transient
hyperbilirubinemia**



Causes:

Due to accelerated hemolysis and an immature hepatic system for the uptake, conjugation, and secretion of bilirubin



2- Neonatal “Physiological Jaundice”

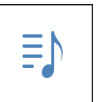
- **UCB** in the blood **increases** more than the binding capacity of albumin (**20-25 mg/dl**) (acholuric jaundice)
- **UCB** cross the blood-brain barrier, cause toxic **encephalopathy** (**kernicterus**)
- If left untreated, may result in **mental retardation**



2- Neonatal “Physiological Jaundice”

Treatment:

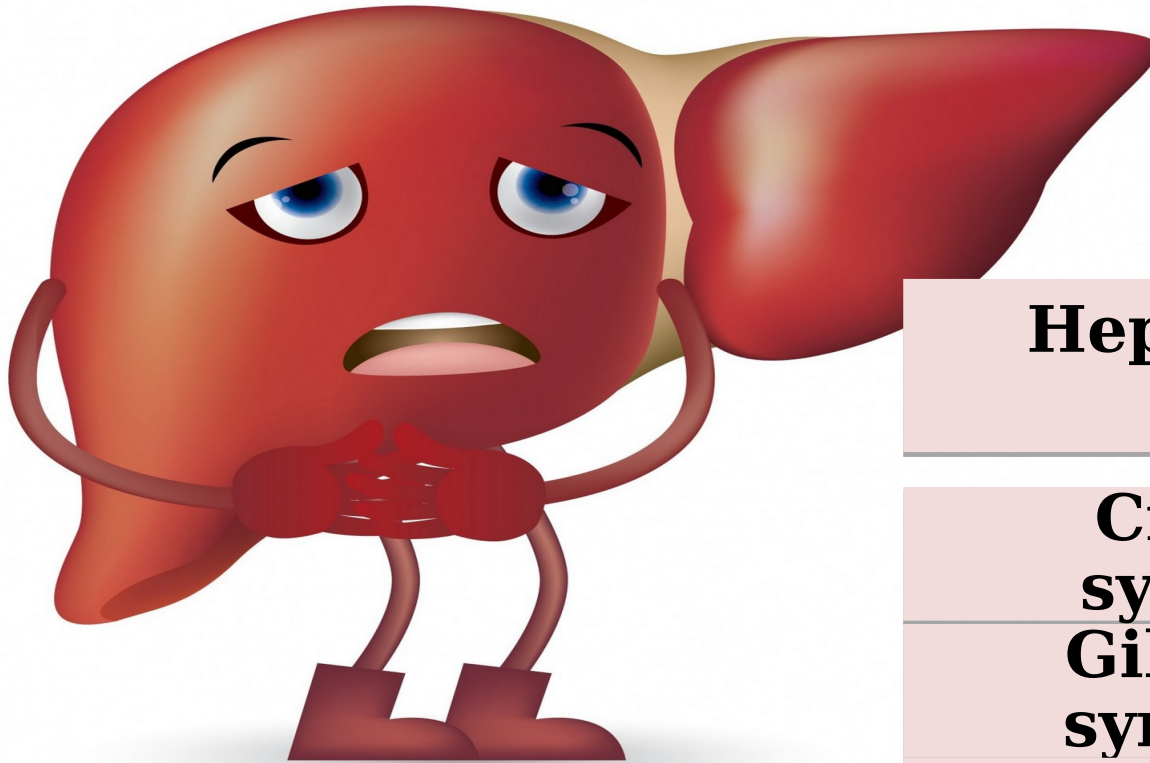
- 1- **Phototherapy (blue light)**: converts bilirubin to more polar water-soluble isomers
- 2- **Barbiturates**: induction of bilirubin UDP-glucuronosyl transferase enzyme



Hepatic Jaundice



B- Hepatic Jaundice



**Hepatocellular -1
damage**

**Crigler-Najjar -2
syndromes I & II**

**Gilbert -3
syndrome**

**Dubin-Johnson -4
syndrome**

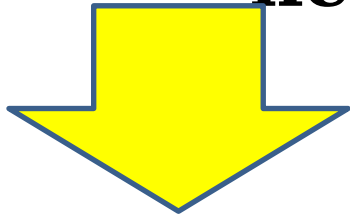
**Rotor -5
syndrome**



1- Hepatocellular damage

Causes:

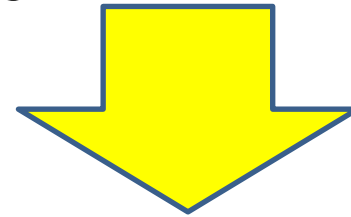
Toxins, drugs,
hepatitis viruses and
cirrhosis



Damage to liver
cells and
decreased
conjugation
capacity



Increase of **UCB**
levels the **blood**



Inflammatory
oedema of
hepatocytes with
compression of the
intracellular
canaliculi



“mild
obstruction”
Increase of **CB**
levels the **blood**



2- Crigler-Najjar syndrome

- It occurs due to **mutation** in the gene encoding **UDP-glucuronyl-transferase** enzyme

Type I Crigler-Najjar: **Complete** absence of the enzyme activity

Type II Crigler-Najjar: **Partial** absence of the enzyme activity (about 10% of the enzyme activity retained)

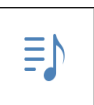


Type I Crigler-Najjar syndrome:

- **Autosomal recessive** disorder due to mutation in the gene encoding UDP-glucuronyl-transferase enzyme
- **Complete** absence of the enzyme activity
- Serum UCB usually exceeds **20 mg/dl**
- **Severe** congenital **jaundice** and **brain damage**
- The disease is often **fatal** within the first 15 months of life

Treatment:

- **Phototherapy** reduces plasma bilirubin levels



Type II Crigler-Najjar syndrome:

- **Autosomal dominant** disorder due to mutation in the gene encoding UDP-glucuronyl-transferase enzyme
- **Partial** absence of the enzyme activity (typically <10% of normal)
- Serum UCB doesn't exceed **20 mg/dl**
- Usually **survives** up to adulthood

Treatment:

- **phenobarbital** treatment is effective, generally with a decrease of at least 25% in serum bilirubin



3- Gilbert's syndrome

- **Autosomal dominant or recessive** disorder due to mutation in the gene encoding UDP-glucuronyl-transferase enzyme
- **Reduced activity** of the enzyme (30% of normal activity is retained)
- Serum **UCB** doesn't exceed **5 mg/dl**
- Episodes of jaundice may be triggered by **stress**

Treatment:

- Very **benign** condition, **NO** treatment is needed

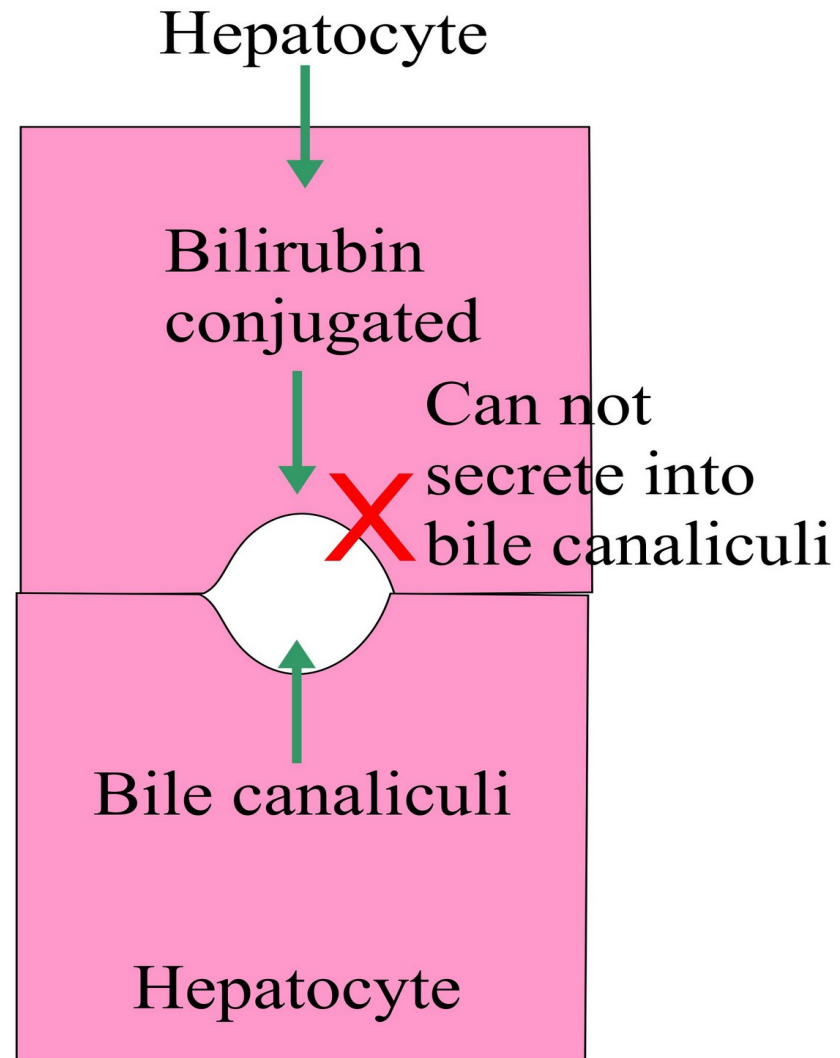
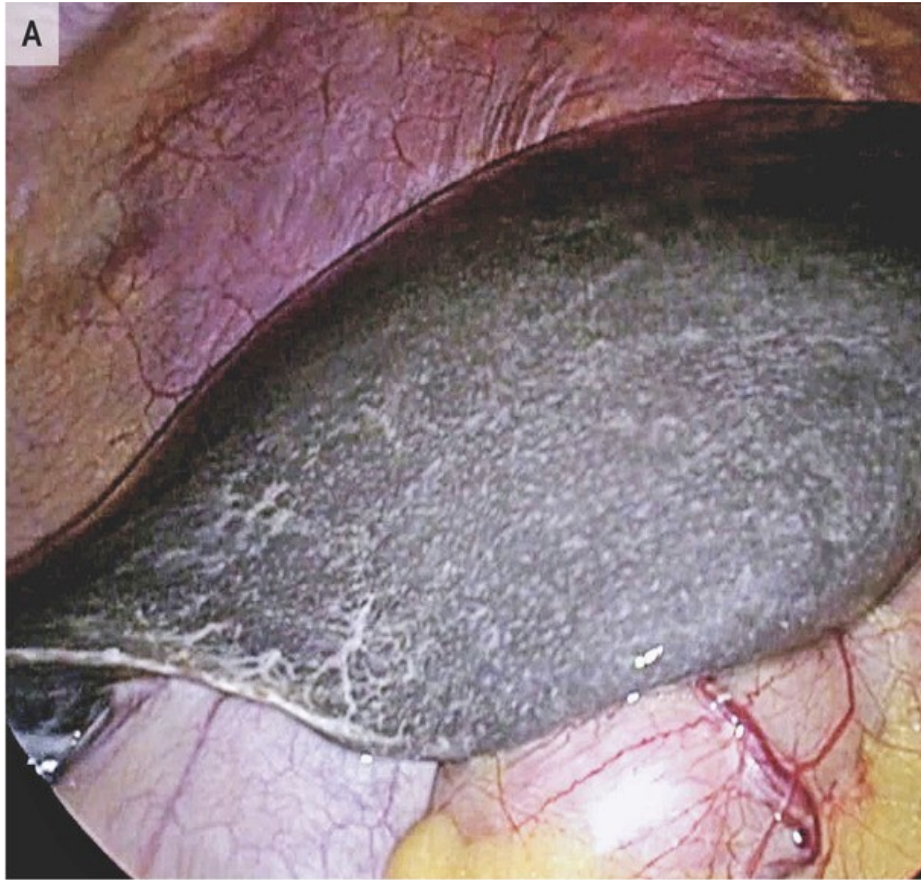


4- Dubin Johnson syndrome

- **Autosomal recessive** disorder caused by mutations in the gene encoding the protein involved in the **secretion** of conjugated bilirubin **into bile**
- It causes a **black liver** due to the deposition of a dark pigment but not bilirubin
- Elevation of **conjugated** bilirubin
- A **benign** condition



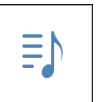
4- Dubin Johnson syndrome



Liver with black pigmentation

5- Rotor syndrome

- **Autosomal recessive** disorder, but its cause has not been identified
- Similar to Dubin-Johnson syndrome, but the liver cells are not pigmented
- Elevation of **conjugated** bilirubin
- A **benign** condition



Impaired glucuronyl transferase activity is observed in all of the following except:

A. Gilbert syndrome

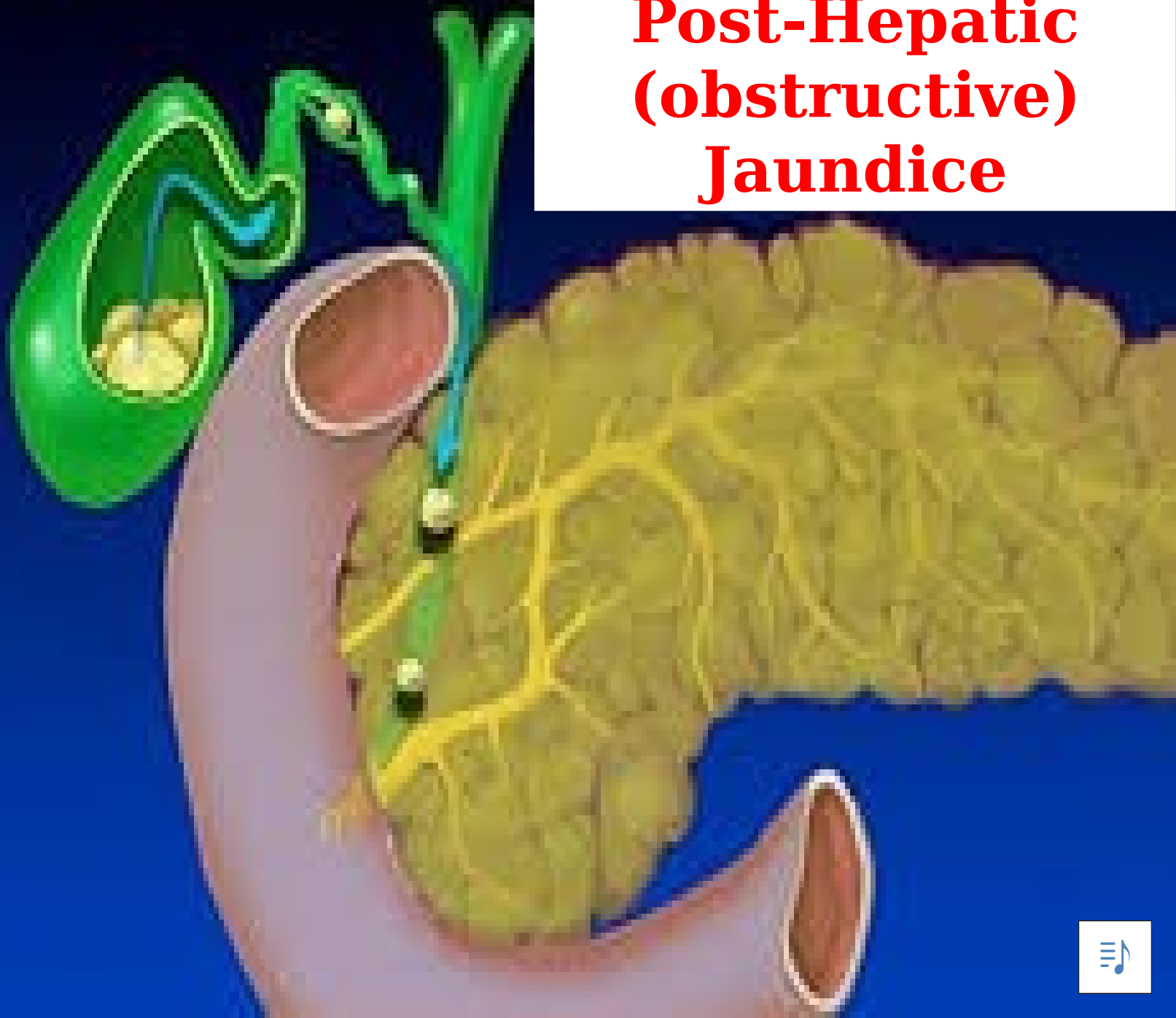
B. Crigler Najjar syndrome

C. Physiological jaundice

D. Dubin Johnson syndrome

E. Hepatocellular jaundice

Post-Hepatic (obstructive) Jaundice

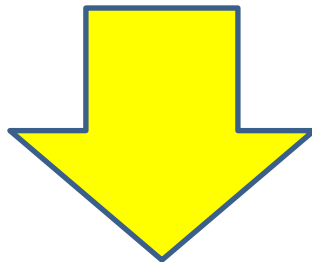


Obstructive Jaundice (Regurgitation)

(hyperbilirubinemia)

Due to **obstruction** of the hepatic or common bile ducts as in case of:

- **Gall stones,**
- **Cancer head of pancreas**
- **Biliary cirrhosis,**
- **Hepatoma**



Preventing passage of **CB** into the
intestine

Obstructive Jaundice



The liver “**regurgitates**” conjugated bilirubin into the blood

The **conjugated** bilirubin is excreted in the
urine
(**choluric jaundice**)

Urinary **urobilinogen** is **absent**

Stool **stercobilinogen** is **absent**,
giving a pale, clay colored stool



MCQ

- **A rise in serum "direct" bilirubin would be expected in all of the following except:**
 - 1. hemolytic jaundice.**
 - 2. absence of glucuronyl transferase as in the newborn.**
 - 3. Gilbert's syndrome.**
 - 4. Type 1 Crigler-Najjar syndrome**
 - 5. biliary obstruction.**



Classification of hyper-bilirubinemia according to site of defect

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Obstruction of the biliary tree



jaundice Obstruction of bile duct	Defect in conjugation and/or excretion of bilirubin in bile			Increase bilirubin production	
Biliary stones Cancer head of pancreas	1.Gilbert syndrome 2.Crigler-najjar syndrome	Dubin-johnson syndrome Rotor syndrome	Hepatic damage e.g; Hepatitis	1.Hemolysis of RBCS as in sickle cell anemia, G6PD deficiency and RH incompatibility 2.Neonatal jaundice	Causes:
Direct (conjugated)	Indirect	Direct	Indirect + direct	Indirect (unconjugated)	Type of elevated bilirubin
Present (Choluric)			Present (Choluric)	Absent (Acholuric) Normal color	<u>Urine</u> 1.Presence of conjugated bilirubin (dark colored urine) 2.Urobilinogen
Absent			Decrease	Increase	
Pale clay colored and bulky(steatorrhea)			Pale clay colored	Normal	<u>Stool</u> 1.Color and consistency
Absent			Decrease	Increase	2.Stercobilin
Normal Increased Present (itching)			Increased	Normal	<u>Blood test:</u> S. ALT and AST Serum ALP Serum bilirubin tests
New Five Year Program			GIT Module		



Type of Bilirubin

Unconjugated

Neonatal "physiological" jaundice

Hemolysis

Gilbert syndrome

Crigler-Najjar syndromes types I & II

Hepatic damage

Conjugated

Obstruction of the biliary tree

Dubin-Johnson syndrome

Rotor syndrome

Hepatic damage



Summary

- **Hemolytic Jaundice (Retention hyperbilirubinemia) is due to overproduction of bilirubin**
- **Impaired glucuronyl transferase activity occurs in**
 - Gilbert syndrome**
 - Crigler Najjar syndrome**
 - Physiological jaundice**
 - Hepatocellular jaundice**

Thank
you

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